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CONNOLLY BOVE LODGE & HUTZ, LLP
P O BOX 2207
WILMINGTON, DE 19899

EXAMINER

CHOWDHURY, IQBAL HOSSAIN

ART UNIT PAPER NUMBER

1652

DATE MAILED: 07/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/525,907	Applicant(s) KROGER ET AL.	
	Examiner Iqbal Chowdhury, Ph.D.	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 April 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) 13, 15 and 16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12 and 14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|-------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>02/05, 12/05</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This application is a 371 of PCT/EP03/09451 filed on 8/26/2003.

The preliminary amendment filed on 2/25/2005 amending claims 1, 3, 5-7, 9-14 is acknowledged. Claims 1-16 are pending.

Applicant's election with traverse of Group I, Claims 1-14, drawn to a process for fermentative production of L-methionine by using Coryneform bacteria comprising a gene having methylenetetrahydrofolate reductase (metF) activity, invention (A) the protein of SEQ ID NO: 2 or a nucleic acid encoding SEQ ID NO: 2 and lysC gene as a species in the response filed on 4/24/2006 is acknowledged.

The traversal is on the ground(s) that restriction between Group I and II is not proper and unity of invention exists. Applicants argue that the present invention is a method of fermentative production of sulfur-containing fine chemicals by culturing L-methionine producing bacteria. Applicant arguments have been fully considered but are not deemed persuasive to withdraw the restriction requirement as previously described.

Applicants arguments regarding special technical feature of the methods claim is not persuasive because Bathe et al. (DEGUSSA AG, WO02/10206 A2, publication 2/7/2002, see IDS) disclose a method of producing L-methionine, a sulfur-containing fine chemical, using Coryneform bacteria expressing metF gene, which is published before the foreign priority date. Further evidence of the lack of special technical feature is presented in the rejection under USC 102 and 103 heading. Therefore, method of producing methionine (Group I), a sulfur-containing

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fine chemical and use of methionine for making animal feed (Group II) lack special technical feature and lack of unity is proper based on the prior art.

Applicant's also argue that Restriction of protein sequence is inappropriate and further stating that proteins of Group (A) to (Z) to (AA), wherein total 27 protein sequences, used in the methods claims, are all examples of metF protein that can be expressed as the heterologous protein and searching of individual metF protein is not required, which is not found persuasive. As discussed in detail in the previous office action proteins of Group (A) to (AA) are all structurally and functionally independent and distinct isolated from different species of microorganisms having different nucleic acid and amino acid sequence and having different metF activity, which are known in the prior art as well as the method of producing methionine (see Bathe et al. document) and all the sequences lack special technical feature among each other. The searching of all the 27 protein sequences and 27 nucleic acid sequences would create a large burden on the office because a search for each of the sequences would not be done solely by searching electronic sequence databases as such databases seldom provide extensive coverage of all variants which are known or have been made of a single protein such that word searching for each variant is required. Such searching would likely be different for each variant as each change may have distinct effects. Furthermore, even sequence searching of the 54 different sequences would be a substantial burden on the office as each sequence has to be examined individually to determine if it includes any variants and reference teaching one such variant would neither anticipate nor make obvious any of the other 52 sequences. As such the novelty and non-obviousness of each variant would have to be addressed individually creating a large burden on the office.

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"For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP 808.02." (see MPEP 803).

The requirement is still deemed proper and is therefore made FINAL.

Claims 13, 15 and 16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in communication filed on 4/24/2006.

Claims 1-12 and 14 are under consideration and are being examined herein.

Priority

Acknowledgement is made of applicants claim for foreign priority of Germany 102-39-308.7 of 8/27/2002.

Claim Objections

Claims 2-14 are objected to because of the recitation "A method ---", which refers to a previous claim. "A method ---" should be changed to "The method ---". Appropriate correction is required.

Claims 5-6 and 12 are objected to as encompassing non-elected subject matter. Appropriate correction is required.

Claim 11 is objected to because of the recitation "is at least partially switched off", which is non-standard jargon. Is this synonymous with eliminated? Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 5 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the present instance, claims 5 and 6 recite “nucleotide sequence homologous thereto” which is unclear as to how similar to the recited sequence, a gene or protein must be to be within the scope of the phrase “homologous thereto”.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12 and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a method producing any sulfur-containing fine chemical using Coryneform bacteria expressing any metF gene. The specification teaches the structure of only a single representative species of such sulfur-containing fine chemical. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than methionine, a single representative species of such sulfur-containing fine

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chemical. Given this lack of description of representative species encompassed by the genus of sulfur-containing fine chemical used in the methods of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 1-12 and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-2 and 14 are directed to a method for the fermentative production of sulfur containing fine chemical by culturing Coryneform bacteria comprising a genus of a DNA molecule encoding methylenetetrahydrofolate reductase (metF) protein or any DNA molecule encoding any metF protein. Claim 1 recites that the sulfur containing fine chemical would be concentrated from culture medium or from bacterial cells followed by the isolation of the produced said sulfur containing fine chemical from culture media or from bacterial cell. Claim 2 recites that the said sulfur containing fine chemical is L-methionine, and claim 3 recites that the said heterologous metF gene nucleic acid sequence is less than 100% homologous to metF gene nucleic acid sequence derived from Coryneform glutamicum ATCC 13032 and claim 4 recites that metF gene can be isolated from various microorganisms as disclosed in claim 4. Claim 7 recites that the said metF sequence is DNA or RNA, which can be replicated in Coryneform bacteria or is stably integrated into chromosome and claim 8 recites that bacteria transformed with a plasmid comprising at least one copy of metF gene under control of regulatory sequence,

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wherein metF gene is integrated into bacterial chromosome. Claim 9 recites that the metF encoded protein is over-expressed and claim 10 recites that the bacteria wherein at least one additional gene of biosynthetic pathway of the desired sulfur containing fine chemicals has been amplified or mutated such that its activity is not influenced by metabolic metabolites. Claim 11 recites that the bacteria wherein at least one metabolic pathway, which reduces the production of the desired sulfur containing fine chemical, is partially switched off. Claim 12 recites bacteria wherein at least one gene from recited fifteen genes would be over-expressed. Claim 14 recites that the microorganism is the *Coryneform glutamicum*. As discussed in the written description guidelines the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species, which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The specification teaches the structure of only several representative species of metF gene and a single representative species of lysC gene. The specification also teach a single method of amplification of an additional gene of biosynthetic pathway of sulfur-containing chemical by a *C. glutamicum* strain transformed with lysC gene and over-produced lysC encoding aspartate kinase and mutated the lysC at position 311 by altering threonine residue to isoleucine by a

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single method of site directed mutagenesis, wherein lysC gene is resistant to metabolic metabolite such as threonine.

Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of encoding the polypeptide having methylenetetrahydrofolate reductase (metF) activity (claim 1) or any genes encoding any enzymes of claim 12. The specification also failed to describe any or all genes of biosynthetic pathway of any sulfur-containing chemicals, which are either amplified or mutated (claim 10). The specification also fails to teach how the genes are amplified or mutated as such the activity of the genes are not influenced by any metabolite of any metabolic pathway (claim 10). In addition, the specification also totally fails to describe any methods to switch off the metabolic pathway, which involved in the reducing the sulfur-containing fine chemicals (claim 11).

Given this lack of description of representative species encompassed by the genus of DNAs used in the methods of the claim, and the methods of expressing additional genes of sulfur-containing fine chemical biosynthetic pathway or any methods of amplifying or mutating any gene, or any method of switch off a metabolic pathway, which contain numerous genes, by any means to reduce the degradation of sulfur-containing fine chemicals, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 1-12 and 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for fermentative production of L-methionine by culturing Coryneform bacteria comprising a DNA molecule encoding the

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methylenetetrahydrofolate reductase (metF) protein of SEQ ID NO: 2 from Coryneform diphtheria, does not reasonably provide enablement for- 1) a method for producing any sulfur-containing fine chemicals by culturing any Coryneform bacteria, 2) a method for producing any sulfur-containing fine chemicals by culturing any Coryneform bacteria comprising any DNA molecule encoding any methylenetetrahydrofolate reductase (metF) protein, 3) any genes or all genes of the biosynthetic pathway of any sulfur-containing fine chemicals, which will be amplified or mutated, and 4) any metabolic pathway comprising numerous genes, which reduce the production of sulfur-containing fine chemical would be switched off. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 1 is so broad as to encompass a method for producing any sulfur-containing fine chemical using Coryneform bacteria expressing any metF gene. The specification teaches the structure of only a single representative species of such sulfur-containing fine chemical.

Claims 1 and 3 are so broad as to encompass a method for producing any sulfur-containing fine chemicals by culturing any Coryneform bacteria comprising any DNA molecule encoding any methylenetetrahydrofolate reductase (metF) protein from any source. Claim 1 recites that the sulfur containing fine chemical would be concentrated from culture medium or from bacterial cells followed by the isolation of the produced said sulfur containing fine chemical from culture media or from bacterial cell. Claim 2 recites that the said sulfur containing fine chemical is L-methionine, and claim 3 recites that the said heterologous metF gene nucleic acid sequence is less than 100% homologous to metF gene nucleic acid sequence derived from

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Coryneform glutamicum ATCC 13032. Claim 7 recites that the said metF sequence is DNA or RNA, which can be replicated in Coryneform bacteria or is stably integrated into chromosome and claim 8 recite that bacteria transformed with a plasmid comprising at least one copy of metF gene under control of regulatory sequence, wherein metF gene is integrated into bacterial chromosome. Claim 9 recites that the metF-encoded protein is over-expressed. Claim 14 recites that the microorganism is the Coryneform glutamicum.

Claim 10 is so broad as to encompass a method for producing any sulfur-containing fine chemicals by culturing any Coryneform bacteria comprising any DNA molecule encoding any methylenetetrahydrofolate reductase (metF) protein, wherein the bacteria comprises at least one additional gene of the biosynthetic pathway of the desired any sulfur containing fine chemicals has been amplified or mutated by using any methods such that its activity is not influenced by any metabolites of any metabolic pathways.

Claim 11 is so broad as to encompass a method for producing any sulfur-containing fine chemicals by culturing any Coryneform bacteria comprising any DNA molecule encoding any methylenetetrahydrofolate reductase (metF) protein, wherein the bacteria comprises at least one gene from recited fifteen genes would be over-expressed.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of sulfur-containing fine chemicals broadly encompassed by the claims. The specification teaches the structure of only a single representative species of such sulfur-containing fine chemical.

The scope of the claims is also not commensurate with the enablement provided by the disclosure with regard to the extremely large number of methylenetetrahydrofolate reductase

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(metF) gene broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only several methylenetetrahydrofolate reductase (metF) genes.

The scope of the claims is also not commensurate with the enablement provided by the disclosure with regard to the extremely large number of genes which would be required to be expressed or mutated in the said microorganism for the production of sulfur-containing fine chemicals broadly encompassed by the claims (claim 12). Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to several additional genes, one gene from each genus, and also discloses only single representative gene lysC, which will be mutated by site directed mutagenesis type of mutation, which is required to be expressed in the said microorganism for the production of L-threonine, such that L-threonine does not influence as a feed back inhibitor.

The scope of the claims is also not commensurate with the enablement provided by the

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disclosure with regard to the amplification and mutating at least one gene of the sulfur containing fine chemicals biosynthetic pathway, which comprises numerous genes, such that its activity is not influence by metabolites of any metabolic pathway (claim 10). Since the method of mutating a gene requires a knowledge of and guidance with regard to the mutation of which amino acids in the specific protein's sequence to be mutated, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure totally lacks full scope of the claimed invention such as- 1) what are the genes of the sulfur-containing fine chemicals biosynthetic pathway, how they are amplified and how they are mutated?

The scope of the claims is also not commensurate with the enablement provided by the disclosure with regard to the metabolic pathway, which comprises numerous genes that reduces the production of sulfur-containing fine chemical would be switched off (claim 11). However, in this case, the disclosure totally lacks full scope of the claimed invention such as- 1) what are the genes of the sulfur-containing fine chemicals metabolic pathway, and 2) how the genes are switched off to reduce the production of sulfur-containing fine chemicals.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple point mutations or substitutions.

The specification does not support the broad scope of the claims which encompass a method for producing any sulfur-containing fine chemicals by culturing any Coryneform bacteria comprising any DNA molecule encoding any methylenetetrahydrofolate reductase (metF) protein because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting methylenetetrahydrofolate reductase activity; (B) the general tolerance of methylenetetrahydrofolate reductase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any methylenetetrahydrofolate reductase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

The specification does not support the broad scope of the claims which encompass a method for producing any sulfur-containing fine chemicals by culturing any Coryneform bacteria expressing any metF protein because the specification does **not** establish a rational and predictable scheme for producing any sulfur-containing fine chemicals in the bacterial host expressing metF gene and the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

The specification does not also support the broad scope of the claims which encompass a method for producing any sulfur-containing fine chemicals by culturing any Coryneform bacteria comprising over-expressing any lysC DNA molecule (claims 10 and 12) encoding any aspartate kinase protein because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting kinase activity; (B) the general tolerance of lysC to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying

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any lysC residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

The specification does not also support the broad scope of the claims which encompass a method for producing any sulfur-containing fine chemicals by using Coryneform bacteria amplifying any gene of sulfur-containing fine chemical biosynthetic pathway or mutating any gene of sulfur-containing fine chemical biosynthetic pathway by any means such that the activity of the gene is not influenced by metabolites of metabolic pathway because the specification does not establish a rational and predictable scheme for amplifying any gene of sulfur-containing fine chemical biosynthetic pathway or mutating any gene of sulfur-containing fine chemical biosynthetic pathway in the bacterial host expressing metF gene and the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

The specification also does not support the broad scope of the claims which encompass a method of producing methionine, a sulfur-containing fine chemical, by using a microorganism, wherein the microorganism is modified by a series of methods to eliminate one of the metabolic pathway, which reduces the production of said methionine (claim 11) because the specification does not establish: (A) the way of modifying the microorganism by eliminating some of the metabolic pathways, (B) the general tolerance of the microorganism to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying of microorganism by modifying any pathways as recited in claim 11 with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the

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essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a method for producing any sulfur containing fine chemicals by culturing any Coryneform bacteria comprising any DNA molecule encoding any methylenetetrahydrofolate reductase (metF) protein. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of a method for producing any sulfur-containing fine chemicals by culturing any Coryneform bacteria comprising any DNA molecule encoding any methylenetetrahydrofolate reductase (metF) protein having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country. more than one year prior to the date of application for patent in the United States.

Claims 1-6, 7-8, 9-10-12 and 14 are rejected under 35 U.S.C. 102 (b) as being anticipated by Bathe et al. (DEGUSSA AG, WO02/10206 A2, publication 2/7/2002, see IDS). Bathe et al. disclose the sequence of a metF protein (SEQ ID NO: 2) having 349 amino acids residues from

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Corynebacterium glutamicum, which is 70% identical to the SEQ ID NO: 2 of the instant application. Bathe et al. also disclose method for producing L-methionine, a sulfur-containing fine chemical by using *Corynebacterium glutamicum* transformed with metF gene of SEQ ID NO: 1 or variants thereof, wherein metF gene expression is enhanced, culturing the recombinant bacteria, concentrating L-methionine from culture media or from cell and isolated L-methionine. Bathe et al. further disclose that the said bacteria wherein additional genes of L-methionine biosynthesis pathway including lysC gene is enhanced, mutating the said gene such that lysC gene is feed back resistant to metabolic metabolite and produce enhanced production of desired L-methionine. Bathe et al. also disclose that the DNA and RNA are replicated into the *Coryneform* bacterium. Bathe et al. further disclose that the metabolic pathway, which reduces the production of L-amino acid, is eliminated. Claims 5 and 6 are rejected because of the recitation “ or a nucleotide sequence homologous thereto”, which broadened the scope of the claim to any nucleotide sequence encoding a protein having metF activity.

Claims 1-6, 7-8, 9-10, 11, 12 and 14 are rejected under 35 U.S.C. 102 (b) as being anticipated by Bathe et al. (US PG PUB 2002/0110877, publication 8/15/2002, see IDS). Bathe et al. disclose the sequence of a metF protein (SEQ ID NO: 2) having 349 amino acids residues from *Corynebacterium glutamicum*, which is 70% identical to the SEQ ID NO: 2 of the instant application. Bathe et al. also disclose method for producing L-methionine, a sulfur-containing fine chemical by using *Corynebacterium glutamicum* transformed with metF gene of SEQ ID NO: 1 or variants thereof, wherein metF gene expression is enhanced, culturing the recombinant bacteria, concentrating L-methionine from culture media or from cell and isolated L-methionine.

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Bathe et al. further disclose that the said bacteria wherein additional genes of L-methionine biosynthesis pathway including lysC gene is enhanced, mutating the said gene such that lysC gene is feed back resistant to metabolic metabolite and produce enhanced production of desired L-methionine. Bathe et al. furthermore disclose that the metF gene can be replicated in Coryneform bacteria or stably integrated into the chromosome (Claims 7 and 8) and the elimination of at least one metabolic pathway, which reduces the production of sulfur-containing fine chemical (claim 11). Claims 5 and 6 are rejected because of the recitation “ or a nucleotide sequence homologous thereto”, which broadened the scope of the claim to any nucleotide sequence encoding a protein having metF activity.

Conclusion

Status of the claims:

Claims 1-12 and 14 are pending.

Claims 1-12 and 14 are rejected.

No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Iqbal Chowdhury, PhD, Patent Examiner


Art Unit 1652 (Recombinant Enzymes)

US Patent and Trademark Office

Rm. REM 2B69, Mail Box. 2C70

Ph. (571)-272-8137, Fax. (571)-273-8137

IC


REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP 1600
1600